

REPLACEMENT SHEET

Title: IL-15 ANTAGONISTS

Applicant(s): Dreher et al.

Filing Date: April 12, 2005 Serial No.: 10/530,987

Customer No.: 21559

Figure 1 a:

Amino acid sequence WT-IL-15-hIgG1:

NWVNVISDLKKTEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG
DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMF
INTSDPKSADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD
IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEA
LHNHYTQKSLSLSPGK

(SEQ ID NO: 4)

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Figure 1 b:

Amino acid sequence WT-IL-15-mIgG2a:

NWVNVISDLKKTEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESG
DASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMF
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSLSPIVTCVVVD
VSEDDPDVQISWVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPE
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 5)

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Figure 2 a:

Amino acid sequence WT-IL-15:

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG

DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMF

INTS

(SEQ ID NO: 1)

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Figure 2 b:

Amino acid sequence hIgG1:

PKSADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHY
TQKSLSLSPGK

(SEQ ID NO: 2)

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Figure 2 c:

Amino acid sequence mIgG2a:

PRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMI SLSPIVTCVVVDVSEDD
PDVQISW FVNNVEVHTAQTQTHREDYNSTLRVVSALPIQH QDWMSGKEFKCKVNN
KDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTD FMPEDIYVE
WTNNGKTELNYKNTEPVLDSDGSYFMY SKLRVEKKNWVERNSYSCSVVHEGLHNNH
HTTKSFSRTPGK

(SEQ ID NO: 3)

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Figure 3 a:

Amino acid sequence Igk8

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG
DASIHDTVENLIILANNSLSNNGNVTESGCKECEELEEKNIKEFLDSFVHIVDMF
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFFPKIKDVLMLSLSPIVTCVVVD
VSEDDPDVQISWVNNVEVHTAQQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDPMPE
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 24)

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Figure 3 b:

Amino acid sequence 149-Fc

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG
DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLDSFVHIVQMF
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSLSPIVTCVVVD
VSEDDPDVQISWVNNVEVHTAQQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPE
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 25)

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Figure 4:

Nucleic acid sequence WT-IL-15-hIgG1:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAACCGAAGATCTTATTCAATCTA
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGTTGCAAAGT
AACAGCAATGAAGTGCTTTCTCTTGAGATTACAAGTTATTTCACTTGAGTCCGGA
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAACTGGA
GGAAAAAATATTAAAGAATTTTTCAGAGTTTGTACATATTGTCCAAATGTTT
ATCAACACTTCGGATCCCAAATCTGCTGACAAAACCTCACACATGCCCCACCGTGCC
CAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCAAACCCAA
GGACACCCCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTG
AGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGAGGTGC
ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGT
CAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGC
AAGGTCTCCAACAAAGCCC'TCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCA
AAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCT
GACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGAC
ATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGC
CTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGA
CAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCT
CTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGATCTA
GA

(SEQ ID NO: 9)

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Figure 5:

Nucleic acid sequence WT-IL-15-mIgG2a:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTATTCAATCTA
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGTTGCAAAGT
AACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTGAGTCCGGA
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAACTGGA
GGAAAAAATATTAAAGAATTTTTCAGAGTTTTGTACATATTGTC¹CAAATGTTT
ATCAACACTTCGGATCCCAGAGGGCCCAACAATCAAGCCCTGTCTCCATGCAAAT
GCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAGAT
CAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGGTGGTGGAT
GTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAG
TACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGT
GGTCAGTGCCCTCCCCATCCAGCACCAAGGACTGGATGAGTGGCAAGGAGTTCAAA
TGCAAGGTCAACAACAAGACCTCCCAGCGCCCATCGAGAGAACCATCTCAAAAC
CCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCAGAAGAAGA
GATGACTAAGAAACAGGTCACTCTGACCTGCATGGTCACAGACTTCATGCCTGAA
GACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTACAAGAACA
CTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAGCTGAGAGT
GGAAAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTTCAGTGGTCCACGAG
GGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGGTAAATGAG

(SEQ ID NO: 10)

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Figure 6 a:

Nucleic acid sequence WT-IL-15:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTATTCAATCTA
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCAGTTGCAAAGT
AACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTGAGTCCGGA
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAAGTGA
GGAAAAAATATTAAAGAATTTTTGCAGAGTTTGTACATATTGTCCAAATGTTC
ATCAACACTTC

(SEQ ID NO: 6)

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Figure 6 b:

Nucleic acid sequence hIgG1:

CCCAAATCTGCTGACAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCC
TGGGGGGACCGTCAGTCTTCCTCTTCCCCCAAACCCAAGGACACCCTCATGAT
CTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCACGAAGACCCT
GAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAA
AGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGT
CCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAA
GCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG
AACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT
CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGG
GAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTGGACT
CCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA
GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC
ACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAT

(SEQ ID NO: 7)

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Figure 7:

Nucleic acid sequence mIgG2a:

CCCAGAGGGCCCACAATCAAGCCCTGTCTCCATGCAAATGCCCAGCACCTAACC
TCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAAGATCAAGGATGTACTCAT
GATCTCCCTGAGCCCCATAGTCACATGTGTGGTGGTGGATGTGAGCGAGGATGAC
CCAGATGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTACACACAGCTCAGA
CACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTGCCCTCCC
CATCCAGCACCAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAAC
AAAGACCTCCCAGCGCCCATCGAGAGAACCATCTCAAACCCAAAGGGTCAGTAA
GAGCTCCACAGGTATATGTCTTGCCTCCACCAGAAGAAGAGATGACTAAGAAACA
GGTCACTCTGACCTGCATGGTCACAGACTTCATGCCTGAAGACATTTACGTGGAG
TGGACCAACAACGGGAAAACAGAGCTAAACTACAAGAACACTGAACCAGTCCTGG
ACTCTGATGGTTCTTACTTCATGTACAGCAAGCTGAGAGTGGAAAAGAAGAACTG
GGTGGAAAGAAATAGCTACTCCTGTTTCAGTGGTCCACGAGGGTCTGCACAATCAC
CACACGACTAAGAGCTTCTCCCGGACTCCGGGTAAATGAG

(SEQ ID NO: 8)

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Figure 8 a:

Nucleic acid sequence of murine IgK leader:

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCCAGGTTCCA
CTGGTGAC

(SEQ ID NO: 11)

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Figure 8 b:

Nucleic acid sequence of human CD5 leader:

ATGCCCATGGGGTCTCTGCAACCGCTGGCCACCTTGTACCTGCTGGGGATGCTGG

TCGCTTCCTGCCTCGGA

(SEQ ID NO: 12)

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Figure 8 c:

Nucleic acid sequence of human CD4 leader:

ATGAACCGGGGAGTCCCTTTTAGGCACTTGCTTCTGGTGCTGCAACTGGCGCTCC
TCCCAGCAGCCACTCAGGGA

(SEQ ID NO: 13)

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Figure 8 d:

Nucleic acid sequence of human IL-2 leader:

ATGTACAGGATGCAACTCCTGTCTTGCAATTGCACTAAGTCTTGCACTTGTCACAA
ACAGT

(SEQ ID NO: 14)

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Figure 9 a:

Nucleic acid sequence of human MCP leader:

ATGAAAGTCTCTGCCGCCCTTCTGTGCCTGCTGCTCATAGCAGCCACCTTCATTC

CCCAAGGGCTCGCT

(SEQ ID NO: 15)

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Figure 9 b:

Nucleic acid sequence of the short native human IL-15 leader:

ATGTCTTCATTTTGGGCTGTTTCAGTGCAGGGCTTCCTAA

(SEQ ID NO: 16)

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Figure 9 c:

Nucleic acid sequence of the long native human IL-15 leader:

ATGAGAATTTTCGAAACCACATTTGAGAAGTATTTCCATCCAGTGCTACTTGTGTT
TACTTCTAAACAGTCATTTTCTAACTGAAGCTGGCATTTCATGTCCTTCATTTTGGG
CTGTTTCAGTGCAGGGCTTCCTAAACAGAAGCC

(SEQ ID NO: 17)

Figure 10:
Igk8 nucleic acid sequence

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCCAGGTTCCA
CTGGTGACAACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTAT
TCAATCTATGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGT
TGCAAAGTAACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTG
AGTCCGGAGATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAA
CAACAGTTTGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAG
GAACTGGAGGAAAAAATATTAAAGAATTTTGGACAGTTTGTACATATTGTGCG
ACATGTTTCATCAACACTTCGGATCCCAGAGGGCCCAATCAAGCCCTGTCCTCC
ATGCAAATGCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCT
CCAAAGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGG
TGGTGGATGTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAA
CGTGGAAGTACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACT
CTCCGGGTGGTCAGTGCCCTCCCCATCCAGCACCAAGGACTGGATGAGTGGCAAGG
AGTTCAAATGCAAGGTCAACAACAAAGACCTCCCAGCGCCCATCGAGAGAACCAT
CTCAAACCCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCA
GAAGAAGAGATGACTAAGAAACAGGTCCTGACCTGCATGGTCACAGACTTCA
TGCCTGAAGACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTA
CAAGAACACTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAG
CTGAGAGTGGAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTTCAGTGG
TCCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGG
TAAATGAG

(SEQ ID NO: 26)

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Figure 11:

149-Fc nucleic acid sequence

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCAGGTTCCA
CTGGTGACAACCTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTAT
TCAATCTATGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGT
TGCAAAGTAACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTG
AGTCCGGAGATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAA
CAACAGTTTGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAG
GAACTGGAGGAAAAAATATTAAGAATTTTTGGACAGTTTTGTACATATTGTCC
AAATGTTTCATCAACACTTCGGATCCCAGAGGGCCCAATCAAGCCCTGTCTCC
ATGCAAATGCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCT
CCAAAGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGG
TGGTGGATGTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAA
CGTGGAAGTACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACT
CTCCGGGTGGTCAGTGCCCTCCCCATCCAGCACCAGGACTGGATGAGTGGCAAGG
AGTTCAAATGCAAGGTCAACAACAAAGACCTCCCAGCGCCCATCGAGAGAACCAT
CTCAAAACCCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCA
GAAGAAGAGATGACTAAGAAACAGGTCACTCTGACCTGCATGGTCACAGACTTCA
TGCCTGAAGACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTA
CAAGAACACTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAG
CTGAGAGTGGAAAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTCAGTGG
TCCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGG
TAAATGAG

(SEQ ID NO: 27)